DETAILED ACTION

Acknowledgement of Receipt

Applicant's Response, filed 5/9/08, in reply to the Office Action mailed 1/11/08, is acknowledged and has been entered. Claim 1 has been amended. Claims 1-19 are pending and are examined herein on the merits for patentability.

Interview Summary

In a telephonic interview with Mr. Hymel and Mr. Gagnebin on 10/24/08, the examiner indicated that the previous rejection would be withdrawn in view of Applicant's arguments that the Mueller reference teaches a higher salt concentration than that which is claimed. The examiner indicated that a new grounds of rejection would be made under 35 U.S.C. 103 over Queuille (US 4,120,946), which teaches barium sulfate and polyacrylamide (flocculating agent) in Examples 3-6 that do not include ionic dispersants, in view of Brown which teaches the desirablility of a solid barium sulfate formulation. The examiner also indicated that claim 6 would be found allowable over the cited art since Queuille does not teach smectite clay. Agreement was not reached upon incorporation of claim 6 into claim 1, and Applicant's representatives requested to receive an Office Action.

However, upon preparation of this Office Action, additional prior art was found with regard to claim 6 and grounds for rejection are presented herein.

Response to Arguments

Applicant's arguments, see pages 6-10 of the Response, with respect to the rejection of claims 1-4, 6-10 and 19 under 35 U.S.C. 103(a) as being unpatentable over Mueller (DD238530) in view of Brown (US 3,236,735) have been fully considered and are persuasive. Therefore the rejection has been withdrawn in view of Applicant's demonstration that the ionic content of Mueller's formulation is greater than that which is claimed. However, new grounds for rejection are presented in view of a different interpretation of previously applied references.

Applicant's arguments, see pages 10-11 of the Response, with respect to the rejection of claims 1-10 and 19 under 35 U.S.C. 103(a) as being unpatentable over Mueller (DD238530) in view of Brown (US 3,236,735), further in view of Ruddy (US 5,466,440) have been fully considered and are persuasive. Therefore the rejection has been withdrawn.

Applicant's arguments, see page 11 of the Response, with respect to the rejection of claims 1-10 and 12-19 under 35 U.S.C. 103(a) as being unpatentable over Mueller (DD238530) in view of Brown (US 3,236,735), further in view of Vining (US 6,083,162) have been fully considered and are persuasive. Therefore the rejection has been withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 7-10 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Queuille *et al.* (US 4,120,946) in view of Brown (US 3,236,735).

Queuille discloses pharmaceutical compositions for barium opacification of the digestive tract, comprising colloidal barium sulfate and polyacrylamide (Bozefloc PL 2169, i.e. a flocculating agnet) in an aqueous vehicle (abstract). See Examples 3-6, which include barium sulfate, polyacrylamide, silicone, methyl parahydroxybenzoate, ethylparahydroxybenzoate and aqueous excipient. Such formulations are free of ionic components. Regarding claim 8, the formulations of Queuille contain silicone, which Applicant defines as an anticaking agent. Regarding claim 7, the formulations of

Queuille may contain kelzan, i.e. xanthan gum (see column 2, line 53), which Applicant defines as a viscosity modifier.

Queille does not specifically teach a solid formulation. It is for this reason that Brown is joined.

Brown teaches formulations comprising barium sulfate for use as x-ray contrast media (column 1, lines 10 – 13). The formulations may be provided as a liquid, or a dry composition containing both barium sulfate and additives is particularly convenient and economical to store and ship. Such a composition is primarily used for the preparation of suspensions having a predetermined barium sulfate content, since the concentrations of the additives in the aqueous medium of the suspension are somewhat critical while the proportions of barium sulfate and additives in the dry composition are necessarily fixed. Such a dry composition may be prepared by combining the required proportions of barium sulfate and additives using a convenient amount of water, and then removing the water by drying, as for example by spray- or film-drying the initial suspension. The resulting dry product consists of barium sulfate particles coated with the additives. The final suspension is then easily prepared as needed by stirring the dry composition into the required amount of water. A dry composition may also be prepared by blending the dry ingredients in the conventional manner, but there is some advantage to using a wet process, as outlined above, since a more even distribution of all ingredients is thereby obtained. If preferred, a dry composition may also be prepared consisting essentially of the additives. This composition may then be mixed with an appropriate proportion of barium sulfate and of water to form the final barium sulfate containing composition.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to provide the formulations of Queuille in the form of a solid. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so, because Brown specifically teaches that dry formulations comprising barium sulfate intended for use as contrast media are particularly convenient and economical to store and ship (column 2, lines 57 – 59). One would have had a reasonable expectation of success in doing so because Brown teaches a variety of methods of preparation of such dry compositions from aqueous solution, such as combining the required proportions of barium sulfate and additives using a convenient amount of water, and then removing the water by drying, as for example by spray- or film-drying the initial suspension.

Regarding claim 1, it is noted that the functional recitation wherein "0.25 g. of said stool marker formulation is diluted with water to 50 ml and titrated against 3.0% w/v ferrous sulfate at pH 5.0-5.55 has a flocculation resistance of less than 5 ml," has not been given patentable weight to distinguish over Queuille. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same functional characteristics of the claimed product. The claims are descriptive and thus would be an inherent property of the claimed composition. In the absence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int.

1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). Since Queuille teaches a composition comprising the same components as those claimed (i.e. barium sulfate, flocculating agent (bozefloc), and the absence of ionic dispersant), it is interpreted, absent evidence to the contrary, that the composition would inherently possess the same claimed flocculation properties.

It is further noted that the recitation of the intended use of the formulation as a stool marker has not been given patentable weight to distinguish over Queuille, in view of Brown, because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Regarding claims 2 – 4, the claims are drawn to compositions and not methods, there is no administered dose, and the compositions disclosed by the prior art would be capable of providing the doses as claimed.

Regarding claim 9, it is noted that the instant claims are product claims, not process of making or using claims. The limitation wherein the formulation is treated with high shear stirring and sonification prior to administration appears to be a product-by-process type limitation. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability

is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." See *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Claims 1-5, 7-10 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Queuille *et al.* (US 4,120,946) in view of Brown (US 3,236,735), further in view of Ruddy (US).

The rejection over Queuille in view of Brown is maintained as above. Queuille and Brown do not teach the particle size of the barium sulfate.

Ruddy teaches barium sulfate compositions which are in particle sizes which encompass those claimed, (column 5, lines 50+ and claim 1). Ruddy teaches the use of high shear provides the advantages of decreasing the processing time (column 12, lines 30+).

It would have been obvious to one of ordinary skill in the art to utilize barium sulfate including particles within the claimed size in the formulation of Queuille, because both the formulations of Queuille and Ruddy are intended for use as radiographic contrast media, and one having ordinary skill would have been motivated to utilize particles having the standard particle size when performing such endeavors.

Claims 1- 4, 7-10 and 12-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Queuille *et al.* (US 4,120,946) in view of Brown (US 3,236,735), further in view of Vining (US 6,083,162).

The rejection over Queuille in view of Brown is maintained as above. Queuille and Brown do not specifically teach a method of visualizing the colon via administering the formulation and manipulating data to determine the portion of data due to marked stool to thereby provide a representation of the colon.

Vining teaches methods for generating interactive, three-dimensional renderings of a patient's colon set forth in Figure 1. The patient can be fed a low residue diet combined with a contrast agent (such as a low density barium, for example, 1.5% W/V barium) for about three days. Such a procedure may serve to homogeneously opacify any retained stool so that the image of the feces can then be subtracted from the final display, or at least from selected images, using image processing techniques (column 8, lines 1 – 20). The technique should allow for the discovery of polyps of 1 cm or greater in size in the colon (column 2, line 12), and is performed via use of a helical CT scanner (column 2, line 29).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize the barium sulfate formulations of Queuille and Brown in the methods of Viking. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so because both teach similar barium compositions for use in radiographic imaging and because Queuille teaches his formulation to have advantages such opacification of the colon. Furthermore, it would

have been obvious to optimize the step of administering multiple doses or the time period of administration as a matter of routine experimentation in order to identify the dosage regimen with desirable effectiveness.

Claims 1- 7, 9-10 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis *et al.* (US 5,741,477) in view of Brown (US 3,236,735).

Davis discloses a negative contrast agent for MRI in an aqueous suspension having a quantity of barium sulfate between 25-30 percent and a quantity of bentonte between 2.5-3.5 percent by weight in which a substantial portion of barium sulfate particles have a mean diameter of at least 10 microns (abstract).

Based on Applicant's calculation of the ionic nature of bentonite on page 11 of the 5/9/08 Response, such a formulation would fall below Applicant's claimed upper limit of ionic dispersant (e.g. 5.02×10^{-4} gram equiv of ionic bentonite per gram of barium sulfate, based on 2.5% bentonite and 30% barium). No other ionic dispersants are taught in the formulations.

Regarding claim 7, Davis also discloses xanthan gum (column 7, line 27), which Applicant defines as a viscosity modifier.

Regarding claim 5, Davis teaches that a mean particle size of ten microns would normally have particle sizes that range from three to about forty microns (column 3, lines 27-31).

Davis does not specifically teach a solid formulation. It is for this reason that Brown is joined.

Brown teaches formulations comprising barium sulfate for use as x-ray contrast media (column 1, lines 10 – 13). The formulations may be provided as a liquid, or a dry composition containing both barium sulfate and additives is particularly convenient and economical to store and ship. Such a composition is primarily used for the preparation of suspensions having a predetermined barium sulfate content, since the concentrations of the additives in the aqueous medium of the suspension are somewhat critical while the proportions of barium sulfate and additives in the dry composition are necessarily fixed. Such a dry composition may be prepared by combining the required proportions of barium sulfate and additives using a convenient amount of water, and then removing the water by drying, as for example by spray- or film-drying the initial suspension. The resulting dry product consists of barium sulfate particles coated with the additives. The final suspension is then easily prepared as needed by stirring the dry composition into the required amount of water. A dry composition may also be prepared by blending the dry ingredients in the conventional manner, but there is some advantage to using a wet process, as outlined above, since a more even distribution of all ingredients is thereby obtained. If preferred, a dry composition may also be prepared consisting essentially of the additives. This composition may then be mixed with an appropriate proportion of barium sulfate and of water to form the final barium sulfate containing composition.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to provide the formulations of Davis in the form of a solid. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so, because Brown specifically teaches that dry formulations

comprising barium sulfate intended for use as contrast media are particularly convenient and economical to store and ship (column 2, lines 57 – 59). One would have had a reasonable expectation of success in doing so because Brown teaches a variety of methods of preparation of such dry compositions from aqueous solution, such as combining the required proportions of barium sulfate and additives using a convenient amount of water, and then removing the water by drying, as for example by spray- or film-drying the initial suspension.

Regarding claim 1, it is noted that the functional recitation wherein "0.25 g. of said stool marker formulation is diluted with water to 50 ml and titrated against 3.0% w/v ferrous sulfate at pH 5.0-5.55 has a flocculation resistance of less than 5 ml," has not been given patentable weight to distinguish over Davis. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same functional characteristics of the claimed product. The claims are descriptive and thus would be an inherent property of the claimed composition. In the absence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). Since Davis teaches a composition comprising the same components as those claimed (i.e. barium sulfate, flocculating agent (smectite clay)), and the absence of ionic dispersant), it is interpreted, absent

evidence to the contrary, that the composition would inherently possess the same claimed flocculation properties.

It is further noted that the recitation of the intended use of the formulation as a stool marker has not been given patentable weight to distinguish over Davis, in view of Brown, because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Regarding claims 2 – 4, the claims are drawn to compositions and not methods, there is no administered dose, and the compositions disclosed by the prior art would be capable of providing the doses as claimed.

Regarding claim 9, it is noted that the instant claims are product claims, not process of making or using claims. The limitation wherein the formulation is treated with high shear stirring and sonification prior to administration appears to be a product-by-process type limitation. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior

product was made by a different process." See *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Claim Objections

Claim 11 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS